

U.S. Patent Application No. 10/591,108
Supplemental Preliminary Amendment

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Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Original) A compound of the formula (I)



or a pharmaceutically acceptable salt thereof, wherein

Z is selected from the group consisting of phenyl; naphthyl; indenyl; C₃₋₇ cycloalkyl; indanyl; tetralinyl; decalinyl; heterocycle; and heterobicycle, wherein Z is optionally substituted with one or more R⁸, wherein R⁸ is independently selected from the group consisting of halogen; CN; OH; NH₂; oxo (=O), where the ring is at least partially saturated; R⁹; and R¹⁰;

R⁹ is selected from the group consisting of C₁₋₆ alkyl; O-C₁₋₆ alkyl; and S-C₁₋₆ alkyl, wherein R⁹ is optionally interrupted by oxygen and wherein R⁹ is optionally substituted with one or more halogen independently selected from the group consisting of F; and Cl;

R¹⁰ is selected from the group consisting of phenyl; heterocycle; and C₃₋₇ cycloalkyl, wherein R¹⁰ is optionally substituted with one or more R¹¹, wherein R¹¹ is independently selected from the group consisting of halogen; CN; OH; NH₂; oxo (=O), where the ring is at least partially saturated; C₁₋₆ alkyl; O-C₁₋₆ alkyl; and S-C₁₋₆ alkyl;

R¹, R⁴ are independently selected from the group consisting of H; F; OH; and R^{4a};

R², R⁵ are independently selected from the group consisting of H; F; and R^{4b};

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R^{4a} is independently selected from the group consisting of C₁₋₆ alkyl; and O-C₁₋₆ alkyl, wherein R^{4a} is optionally substituted with one or more halogen independently selected from the group consisting of F; and Cl;

R^{4b} is C₁₋₆ alkyl, wherein R^{4b} is optionally substituted with one or more halogen independently selected from the group consisting of F; and Cl;

R³ is selected from the group consisting of H; and C₁₋₆ alkyl;

Optionally one or more pairs of R¹, R², R³, R⁴, R⁵ independently selected from the group consisting of R¹/R²; R²/R³; R³/R⁴; and R⁴/R⁵ form a C₃₋₇ cycloalkyl ring, which is optionally substituted with one or more of R¹², wherein R¹² is independently selected from the group consisting of F; Cl; and OH;

X is selected from the group consisting of S(O); S(O)₂; C(O); and C(R¹³R¹⁴);

R¹³, R¹⁴ are independently selected from the group consisting of H; F; C₁₋₆ alkyl; R¹⁵; and R¹⁶;

Optionally one or both pairs of R⁵, R¹³, R¹⁴ selected from the group consisting of R⁵/R¹³; and R¹³/R¹⁴ form a C₃₋₇ cycloalkyl ring, which is optionally substituted with one or more R¹⁷, wherein R¹⁷ is independently selected from the group consisting of F; Cl; and OH;

R¹⁵ is selected from the group consisting of phenyl; naphthyl; and indenyl, wherein R¹⁵ is optionally substituted with one or more R¹⁸, wherein R¹⁸ is independently selected from the group consisting of R¹⁹; R²⁰; halogen; CN; COOH; OH; C(O)NH₂; S(O)₂NH₂; S(O)NH₂; C₁₋₆ alkyl; O-C₁₋₆ alkyl; S-C₁₋₆ alkyl; COO-C₁₋₆ alkyl; OC(O)-C₁₋₆ alkyl; C(O)N(R²¹)-C₁₋₆ alkyl; S(O)₂N(R²¹)-C₁₋₆ alkyl; S(O)N(R²¹)-C₁₋₆ alkyl; S(O)₂-C₁₋₆ alkyl; S(O)-C₁₋₆ alkyl; N(R²¹)S(O)₂-C₁₋₆ alkyl; and N(R²¹)S(O)-C₁₋₆ alkyl, wherein each C₁₋₆ alkyl is optionally substituted with one or more halogen independently selected from the group consisting of F; and Cl;

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R¹⁸ is selected from the group consisting of heterocycle; heterobicycle; C₃₋₇ cycloalkyl; indanyl; tertralinyl; and decalinyl, wherein R¹⁸ is optionally substituted with one or more R²², wherein R²² is independently selected from the group consisting of R¹⁸; R²⁰; halogen; CN; OH; oxo (=O), where the ring is at least partially saturated; NH₂; COOH; C(O)NH₂; S(O)₂NH₂; S(O)NH₂; C₁₋₆ alkyl; O-C₁₋₆ alkyl; S-C₁₋₆ alkyl; N(R²³)-C₁₋₆ alkyl; COO-C₁₋₆ alkyl; OC(O)-C₁₋₆ alkyl; C(O)N(R²³)-C₁₋₆ alkyl; N(R²³)-C(O)-C₁₋₆ alkyl; S(O)₂N(R²³)-C₁₋₆ alkyl; S(O)N(R²³)-C₁₋₆ alkyl; S(O)₂-C₁₋₆ alkyl; S(O)-C₁₋₆ alkyl; N(R²³)S(O)₂-C₁₋₆ alkyl; and N(R²³)S(O)-C₁₋₆ alkyl, wherein each C₁₋₆ alkyl is optionally substituted with one or more halogen independently selected from the group consisting of F; and Cl;

R¹⁹ is selected from the group consisting of phenyl; and naphthyl, wherein R¹⁹ is optionally substituted with one or more R²⁴, wherein R²⁴ is independently selected from the group consisting of halogen; CN; COOH; OH; C(O)NH₂; S(O)₂NH₂; S(O)NH₂; C₁₋₆ alkyl; O-C₁₋₆ alkyl; S-C₁₋₆ alkyl; COO-C₁₋₆ alkyl; OC(O)-C₁₋₆ alkyl; C(O)N(R²⁵)-C₁₋₆ alkyl; S(O)₂N(R²⁵)-C₁₋₆ alkyl; S(O)N(R²⁵)-C₁₋₆ alkyl; S(O)₂-C₁₋₆ alkyl; S(O)-C₁₋₆ alkyl; N(R²⁵)S(O)₂-C₁₋₆ alkyl; and N(R²⁵)S(O)-C₁₋₆ alkyl, wherein each C₁₋₆ alkyl is optionally substituted with one or more halogen independently selected from the group consisting of F; and Cl;

R²⁰ is selected from the group consisting of heterocycle; heterobicycle; and C₃₋₇ cycloalkyl; wherein R²⁰ is optionally substituted with one or more R²⁸, wherein R²⁸ is independently selected from the group consisting of halogen; CN; OH; oxo (=O), where the ring is at least partially saturated; NH₂; COOH; C(O)NH₂; S(O)₂NH₂; S(O)NH₂; C₁₋₆ alkyl; O-C₁₋₆ alkyl; S-C₁₋₆ alkyl; N(R²⁷)-C₁₋₆ alkyl; COO-C₁₋₆ alkyl; OC(O)-C₁₋₆ alkyl; C(O)N(R²⁷)-C₁₋₆ alkyl; N(R²⁷)-C(O)-C₁₋₆ alkyl; S(O)₂N(R²⁷)-C₁₋₆ alkyl; S(O)N(R²⁷)-C₁₋₆ alkyl; S(O)₂-C₁₋₆ alkyl; S(O)-C₁₋₆ alkyl; N(R²⁷)S(O)₂-C₁₋₆ alkyl; and N(R²⁷)S(O)-C₁₋₆ alkyl wherein each C₁₋₆ alkyl is optionally substituted with one or more halogen independently selected from the group consisting of F; and Cl;

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R²¹, R²³, R²⁵, R²⁷ are independently selected from the group consisting of H; and C₁₋₆alkyl, which is optionally substituted with one or more of R²⁸, wherein R²⁸ is independently selected from the group consisting of F; Cl and OH;

R⁶, R⁷ are independently selected from the group consisting of H; (C(R²⁹R³⁰))_m-X¹-Z¹; (C(R³¹R³²))_n-X²-X³-Z²; and C₁₋₄ alkyl, which is substituted with one or more R^{29a}, wherein R^{29a} is independently selected from the group consisting of R^{29b}; and Z¹, provided that R⁶, R⁷ are selected so that not both of R⁶, R⁷ are independently selected from the group consisting of H; CH₃; CH₂CH₃; CH₂CH₂CH₃; and CH(CH₃)₂;

R²⁹, R^{29b}, R³⁰, R³¹, R³² are independently selected from the group consisting of H; halogen; CN; OH; NH₂; COOH; C(O)NH₂; S(O)₂NH₂; S(O)NH₂; C₁₋₆ alkyl; O-C₁₋₆ alkyl; N(R^{32a})-C₁₋₆ alkyl; COO-C₁₋₆ alkyl; OC(O)-C₁₋₆ alkyl; C(O)N(R^{32a})-C₁₋₆ alkyl; N(R^{32a})-C(O)-C₁₋₆ alkyl; S(O)₂N(R^{32a})-C₁₋₆ alkyl; S(O)N(R^{32a})-C₁₋₆ alkyl; S(O)₂-C₁₋₆ alkyl; S(O)-C₁₋₆ alkyl; N(R^{32a})S(O)₂-C₁₋₆ alkyl; and N(R^{32a})S(O)-C₁₋₆ alkyl wherein each C₁₋₆ alkyl is optionally substituted with one or more halogen independently selected from the group consisting of F; and Cl;

R^{32a} is selected from the group consisting of H; and C₁₋₆ alkyl, which is optionally substituted with one or more halogen independently selected from the group consisting of F; and Cl;

Optionally one or more pairs of R²⁹, R³⁰, R³¹, R³² independently selected from the group consisting of R²⁹/R³⁰; and R³¹/R³² form a C₃₋₇ cycloalkyl ring, which is optionally substituted with one or more R^{32b}, wherein R^{32b} is independently selected from the group consisting of F; Cl; and OH;

m is 0, 1, 2, 3 or 4;

n is 2, 3 or 4;

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X^1 is independently selected from the group consisting of a covalent bond; - C_{1-6} alkyl-; - C_{1-6} alkyl-O-; - C_{1-6} alkyl-N(R^{33})-; - $C(O)$ -; - $C(O)-C_{1-6}$ alkyl-; - $C(O)-C_{1-6}$ alkyl-O-; - $C(O)-C_{1-6}$ alkyl-N(R^{33})-; - $C(O)O$ -; - $C(O)O-C_{1-6}$ alkyl-; - $C(O)O-C_{1-6}$ alkyl-O-; - $C(O)O-C_{1-6}$ alkyl-N(R^{33})-; - $C(O)N(R^{33})$ -; - $C(O)N(R^{33})-C_{1-6}$ alkyl-; - $C(O)N(R^{33})-C_{1-6}$ alkyl-O-; - $C(O)N(R^{33})-C_{1-6}$ alkyl-N(R^{34})-; - $S(O)_2$ -; - $S(O)$ -; - $S(O)_2-C_{1-6}$ alkyl-; - $S(O)-C_{1-6}$ alkyl-; - $S(O)_2-C_{1-6}$ alkyl-O-; - $S(O)-C_{1-6}$ alkyl-O-; - $S(O)_2-C_{1-6}$ alkyl-N(R^{33})-; and - $S(O)-C_{1-6}$ alkyl-N(R^{33})-; wherein each C_{1-6} alkyl is optionally substituted with one or more halogen independently selected from the group consisting of F; and Cl;

X^2 is selected from the group consisting of -O-; -S-; -S(O)-; S(O)₂-; and -N(R^{35})-;

X^3 is selected from the group consisting of a covalent bond; - C_{1-6} alkyl-; - C_{1-6} alkyl-O-; - C_{1-6} alkyl-N(R^{36})-; - $C(O)$ -; - $C(O)-C_{1-6}$ alkyl-; - $C(O)-C_{1-6}$ alkyl-O-; - $C(O)-C_{1-6}$ alkyl-N(R^{36})-; - $C(O)O$ -; - $C(O)O-C_{1-6}$ alkyl-; - $C(O)O-C_{1-6}$ alkyl-O-; - $C(O)O-C_{1-6}$ alkyl-N(R^{36})-; - $C(O)N(R^{36})$ -; - $C(O)N(R^{36})-C_{1-6}$ alkyl-; - $C(O)N(R^{36})-C_{1-6}$ alkyl-O-; and - $C(O)N(R^{36})-C_{1-6}$ alkyl-N(R^{37})-; wherein each C_{1-6} alkyl is optionally substituted with one or more halogen independently selected from the group consisting of F; and Cl;

Optionally X^2-X^3 are independently selected from the group consisting of -N(R^{35})-S(O)₂-; -N(R^{35})-S(O)-; -N(R^{35})-S(O)₂- C_{1-6} alkyl-; -N(R^{35})-S(O)- C_{1-6} alkyl-; -N(R^{35})-S(O)- C_{1-6} alkyl-O-; -N(R^{35})-S(O)₂- C_{1-6} alkyl-N(R^{36})-; and -N(R^{35})-S(O)- C_{1-6} alkyl-N(R^{36})-; wherein each C_{1-6} alkyl is optionally substituted with one or more halogen independently selected from the group consisting of F; and Cl;

R^{33} , R^{34} , R^{35} , R^{36} , R^{37} are independently selected from the group consisting of H; and C_{1-6} alkyl, which is optionally substituted with one or more halogen independently selected from the group consisting of F; and Cl;

Z^1 , Z^2 are independently selected from the group consisting of Z^3 ; and - $C(R^{37a})Z^{3a}Z^{3b}$;

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R^{37a} is selected from the group consisting of H; and C_{1-6} alkyl, which is optionally substituted with one or more F;

Z^3 , Z^{3a} , Z^{3b} are independently selected from the group consisting of H; T^1 ; T^2 ; C_{1-6} alkyl; C_{1-6} alkyl- T^1 ; and C_{1-6} alkyl- T^2 ; wherein each C_{1-6} alkyl is optionally substituted with one or more R^{37b} , wherein R^{37b} is independently selected from the group consisting of halogen; CN; OH; NH₂; COOH; C(O)NH₂; S(O)₂NH₂; S(O)NH₂; C_{1-6} alkyl; O- C_{1-6} alkyl; N(R^{37c})- C_{1-6} alkyl; COO- C_{1-6} alkyl; OC(O)- C_{1-6} alkyl; C(O)N(R^{37c})- C_{1-6} alkyl; N(R^{37c})-C(O)- C_{1-6} alkyl; S(O)₂N(R^{37c})- C_{1-6} alkyl; S(O)N(R^{37c})- C_{1-6} alkyl; S(O)₂- C_{1-6} alkyl; S(O)- C_{1-6} alkyl; N(R^{37c})S(O)₂- C_{1-6} alkyl; and N(R^{37c})S(O)- C_{1-6} alkyl; wherein each C_{1-6} alkyl is optionally substituted with one or more halogen independently selected from the group consisting of F; and Cl;

T^1 is selected from the group consisting of phenyl; naphthyl; and indenyl; wherein T^1 is optionally substituted with one or more R^{38} ; wherein R^{38} is independently selected from the group consisting of halogen; CN; R^{39} ; COOH; OH; C(O)NH₂; S(O)₂NH₂; S(O)NH₂; COOT³; OT³; ST³; C(O)N(R^{40})T³; S(O)₂N(R^{40})T³; S(O)N(R^{40})T³ and T³.

T^2 is selected from the group consisting of C_{3-7} cycloalkyl; indanyl; tetralinyl; decalinyl; heterocycle; and heterobicycle; wherein T^2 is optionally substituted with one or more R^{41} , wherein R^{41} is independently selected from the group consisting of halogen; CN; R^{42} ; OH; oxo (=O), where the ring is at least partially saturated; NH₂; COOH; C(O)NH₂; S(O)₂NH₂; S(O)NH₂; COOT³; OT³; C(O)N(R^{43})T³; S(O)₂N(R^{43})T³; S(O)N(R^{43})T³; N(R^{43})T³; and T³;

R^{39} is selected from the group consisting of C_{1-6} alkyl; O- C_{1-6} alkyl; S- C_{1-6} alkyl; COO- C_{1-6} alkyl; OC(O)- C_{1-6} alkyl; C(O)N(R^{44})- C_{1-6} alkyl; S(O)₂N(R^{44})- C_{1-6} alkyl; S(O)N(R^{44})- C_{1-6} alkyl; S(O)- C_{1-6} alkyl; S(O)₂- C_{1-6} alkyl; N(R^{44})S(O)₂- C_{1-6} alkyl; and N(R^{44})S(O)- C_{1-6} alkyl; wherein each C_{1-6} alkyl is optionally substituted with one more R^{45} , wherein R^{45} is independently selected from the group consisting of F; COOR⁴⁶; C(O)N(R^{46})R^{47; S(O)₂N(R^{46})R^{47; OR⁴⁶; N(R^{48})R⁴⁷; T³; O-T³; and N(R^{48})-T³;}}

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R^{42} is selected from the group consisting of C_{1-6} alkyl; $O-C_{1-6}$ alkyl; $S-C_{1-6}$ alkyl; $N(R^{48})-C_{1-6}$ alkyl; $COO-C_{1-6}$ alkyl; $OC(O)-C_{1-6}$ alkyl; $C(O)N(R^{48})-C_{1-6}$ alkyl; $N(R^{48})-C(O)-C_{1-6}$ alkyl; $S(O)_2N(R^{48})-C_{1-6}$ alkyl; $S(O)N(R^{48})-C_{1-6}$ alkyl; $S(O)-C_{1-6}$ alkyl; $S(O)_2-C_{1-6}$ alkyl; $-N(R^{48})S(O)_2-C_{1-6}$ alkyl; and $-N(R^{48})S(O)-C_{1-6}$ alkyl; wherein each C_{1-6} alkyl is optionally substituted with one or more R^{45} , wherein R^{45} is independently selected from the group consisting of F; $COOR^{49}$; $C(O)N(R^{49}R^{50})$; $S(O)_2N(R^{49}R^{50})$; $S(O)N(R^{49}R^{50})$; OR^{49} ; $N(R^{49}R^{50})$; T^3 ; $O-T^3$; and $N(R^{49})-T^3$;

R^{40} , R^{43} , R^{44} , R^{48} , R^{47} , R^{49} , R^{50} are independently selected from the group consisting of H; and C_{1-6} alkyl;

T^3 is selected from the group consisting of T^4 ; and T^5 ;

T^4 is selected from the group consisting of phenyl; naphthyl; and indenyl; wherein T^4 is optionally substituted with one or more R^{51} , wherein R^{51} is independently selected from the group consisting of halogen; CN; $COOR^{52}$; OR^{52} ; $C(O)N(R^{52}R^{53})$; $S(O)_2N(R^{52}R^{53})$; C_{1-6} alkyl; $O-C_{1-6}$ alkyl; $S-C_{1-6}$ alkyl; $COO-C_{1-6}$ alkyl; $OC(O)-C_{1-6}$ alkyl; $C(O)N(R^{52})-C_{1-6}$ alkyl; $S(O)_2N(R^{52})-C_{1-6}$ alkyl; $S(O)N(R^{52})-C_{1-6}$ alkyl; $S(O)_2-C_{1-6}$ alkyl; $S(O)-C_{1-6}$ alkyl; $N(R^{52})S(O)_2-C_{1-6}$ alkyl; and $N(R^{52})S(O)-C_{1-6}$ alkyl; wherein each C_{1-6} alkyl is optionally substituted with one more halogen selected from the group consisting of F; and Cl;

T^5 is selected from the group consisting of heterocycle; heterobicycle; C_{3-7} cycloalkyl; indanyl; tetralinyl; and decalinyl; wherein T^5 is optionally substituted with one or more R^{54} , wherein R^{54} is independently selected from the group consisting of halogen; CN; OR^{55} ; oxo ($=O$), where the ring is at least partially saturated; $N(R^{56}R^{56})$; $COOR^{56}$; $C(O)N(R^{56}R^{58})$; $S(O)_2N(R^{56}R^{66})$; $S(O)N(R^{56}R^{58})$; C_{1-6} alkyl; $O-C_{1-6}$ alkyl; $S-C_{1-6}$ alkyl; $N(R^{56})-C_{1-6}$ alkyl; $COO-C_{1-6}$ alkyl; $OC(O)-C_{1-6}$ alkyl; $C(O)N(R^{56})-C_{1-6}$ alkyl; $N(R^{55})-C(O)-C_{1-6}$ alkyl; $S(O)_2N(R^{65})-C_{1-6}$ alkyl; $S(O)N(R^{55})-C_{1-6}$ alkyl; $S(O)_2-C_{1-6}$ alkyl; $S(O)-C_{1-6}$ alkyl; $N(R^{55})S(O)_2-C_{1-6}$ alkyl; and $N(R^{55})S(O)-C_{1-6}$ alkyl; wherein each C_{1-6} alkyl is

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optionally substituted with one more halogen selected from the group consisting of F; and Cl;

R^{52} , R^{53} , R^{55} , R^{56} , are independently selected from the group consisting of H; and C₁₋₆ alkyl;

with the proviso that the following compounds are excluded:

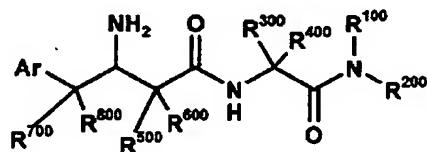
3-amino-N-cyclohexyl-4-phenyl-butyramide,

(S)-3-amino-N-[5-(6-dimethylamino-purin-9-yl)-4-hydroxy-2-hydroxymethyl-tetrahydrofuran-3-yl]-4-p-tolyl-butyramide,

(S)-2-((S)-2-amino-3-phenyl-propane-1-sulfonylamino)-3-phenyl-propionic acid,

(S)-3-amino-4,N-diphenyl-butyramide;

and with the further proviso that compounds according to the following formula are excluded:



wherein

Ar is phenyl optionally substituted with 1, 2, 3, 4, or 5 groups independently selected from halogen; C₁₋₆ alkyl optionally substituted with 1 to 5 halogens; O-C₁₋₆ alkyl optionally substituted with 1 to 5 halogens; and cyano,

R^{500} , R^{600} , R^{700} , R^{800} are independently selected from H; and C₁₋₆ alkyl, optionally substituted by 1 or 2 F,

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R³⁰⁰ and R⁴⁰⁰ are independently selected from hydrogen; C₁₋₆ alkyl, which is optionally substituted by 1 or 2 F; and C₃₋₇ cycloalkyl, optionally substituted by 1, 2, 3, 4 or 5 substituents independently selected from halogen and hydroxy,

R¹⁰⁰ is selected from hydrogen; and C₁₋₆ alkyl, optionally substituted by 1 or 2 F,

R²⁰⁰ is selected from hydrogen; C₁₋₆ alkyl; C₃₋₇ cycloalkyl; phenyl; HET1; C₁₋₆ alkylphenyl; -C₁₋₆ alkyl|AR2; -C₁₋₆ alkyl-C₃₋₇ cycloalkyl; -C₁₋₆ alkyl-HET1; -C₁₋₆ alkyl-HET2; -C₁₋₆ alkyl-CO₂C₁₋₆ alkyl; -C₁₋₆ alkylOCO-C₁₋₆ alkyl; -C₁₋₆ alkylCO-C₁₋₆ alkyl; -C₁₋₆ alkylNHCO-C₁₋₆ alkyl; -C₁₋₆ alkylCONH-alkyl; -C₁₋₆ alkylCON-di-C₁₋₆ alkyl; -C₁₋₆ alkylNH-C₁₋₆ alkyl; -C₁₋₆ alkylN-di-C₁₋₆ alkyl; -C₁₋₆ alkylNHSO₂-C₁₋₆ alkyl; -C₁₋₆ alkylSO₂NH-C₁₋₆ alkyl; -C₁₋₆ alkylSO₂-C₁₋₆ alkyl; and -C₁₋₆ alkylISO₂N-di(C₁₋₆) alkyl;

wherein each C₁₋₆ alkyl is optionally substituted by 1 or 2 F; and

wherein phenyl, AR2, HET1, HET2 and C₃₋₇ cycloalkyl are optionally substituted by 1, 2, 3, 4 or 5 substituents independently selected from phenyl (optionally substituted with halogen, trifluoromethyl, C₁₋₄ alkyl or O-C₁₋₄ alkyl), halogen, C₁₋₆ alkyl, haloC₁₋₆ alkyl, dihaloC₁₋₆ alkyl, trifluoromethyl, O-C₁₋₆ alkyl, carboxy-C₁₋₆ alkyl, carboxy-C₁₋₆ alkoxy, hydroxy, amino, C₁₋₆ alkylamino, diC₁₋₆ alkylamino, -CONH₂, -CONH-C₁₋₆ alkyl, CON-di(C₁₋₆)alkyl, -NHCO-C₁₋₆ alkyl, -SO₂-C₁₋₆ alkyl, SO₂NH₂, -SO₂NH-C₁₋₆ alkyl, SO₂N-diC₁₋₆ alkyl and -NHSO₂-C₁₋₆ alkyl,

further

R¹⁰⁰ and R²⁰⁰ may together with the nitrogen to which they are attached form a ring defined by HET1 or HET3,

wherein a ring comprising R¹⁰⁰ and R²⁰⁰ is optionally substituted by 1 or 2 substituents independently selected from halogen, C₁₋₆ alkyl, O-C₁₋₆ alkyl, cyano, carboxy, carboxy-C₁₋₆ alkyl, -CO₂-C₁₋₆ alkyl, C₁₋₆ alkylamino, di-(C₁₋₆) alkylamino, -NHCO-C₁₋₆ alkyl, -CONH-C₁₋₆ alkyl, -CON-di-C₁₋₆ alkyl and HET1, wherein each C₁₋₆ alkyl group is optionally substituted by 1 or 2 substituents independently selected from hydroxy and fluoro;

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and

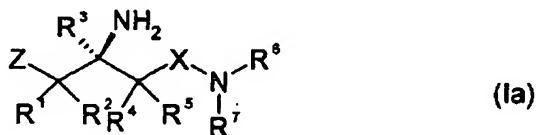
AR2 is a 8-, 9- or 10-membered unsaturated, partially or fully saturated bicyclic carbocyclic ring;

HET1 is a 3-, 4-, 5- or 6-membered, unsaturated, partially or fully saturated monocyclic heterocycll ring containing up to four heteroatoms independently selected from O, N, and S (but not containing any O-O, O-S or S-S bonds) linked via a ring carbon atom or a ring nitrogen atom if the ring is not thereby quaternised, and wherein an available carbon, sulfur or nitrogen atom may be oxidized;

HET2 is a 8-, 9- or 10-membered, unsaturated, partially or fully saturated bicyclic heterocycll ring containing up to four heteroatoms independently selected from O, N, and S (but not containing any O-O, O-S or S-S bonds) and linked via a ring carbon atom in either of the rings comprising the bicyclic system; and

HET3 is a N-linked saturated bicyclic ring system containing up to 12 ring atoms including the linking nitrogen atom.

2. (Original) A compound according to claim 1 of formula (Ia)



or a pharmaceutically acceptable salt thereof, wherein Z, R¹-R⁷ and X have the meaning as indicated in claim 1.

3. (Previously presented) A compound according to claim 1, wherein Z is phenyl or heterocycle.

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4. (Previously presented) A compound according to claim 1, wherein Z is optionally substituted with 1 or 2 R⁸, which are the same or different.
5. (Previously presented) A compound according to claim 1, wherein R⁸ is selected from the group consisting of Cl; F; CN; CH₃; and OCH₃.
6. (Previously presented) A compound according to claim 1, wherein Z is 2-Fluoro-phenyl.
7. (Previously presented) A compound according to claim 1, wherein R¹, R⁴ are independently selected from the group consisting of H; F; OH; CH₃; and OCH₃.
8. (Previously presented) A compound according to claim 1, wherein R², R⁵ are independently selected from the group consisting of H; F; and CH₃.
9. (Previously presented) A compound according to claim 1, wherein R¹, R², R⁴, R⁵ are H.
10. (Previously presented) A compound according to claim 1, wherein R³ is H.
11. (Previously presented) A compound according to claim 1, wherein X is C(O) or S(O)₂.
12. (Previously presented) A compound according to claim 1, wherein R⁶ is selected from the group consisting of H; and CH₃.
13. (Previously presented) A compound according to claim 1, wherein X¹ is a covalent bond.

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14. (Previously presented) A compound according to claim 1, wherein m is 0, 1, 2 or 3.

15. (Previously presented) A compound according to claim 1, wherein R⁷ is Z¹.

16. (Previously presented) A compound according to claim 1, wherein R⁷ is C₁₋₄ alkyl, substituted with 1-4 R^{29a}, which are the same or different.

17. (Original) A compound according to claim 16, wherein R⁷ is selected from the group consisting of CH(R^{29a})₂; CHR^{29a}-CH₂R^{29a}; CH₂CH(R^{29a})₂; CH₂CHR^{29a}-CH₂R^{29a}; and CH₂CH₂CH(R^{29a})₂.

18. (Previously presented) A compound according to claim 1, wherein R^{29a} is selected from the group consisting of R^{29b}; and Z¹; and wherein R^{29b} is selected from the group consisting of H; F; Cl; NH₂; NHCH₃; N(CH₃)₂; CH₃; and C₂H₅.

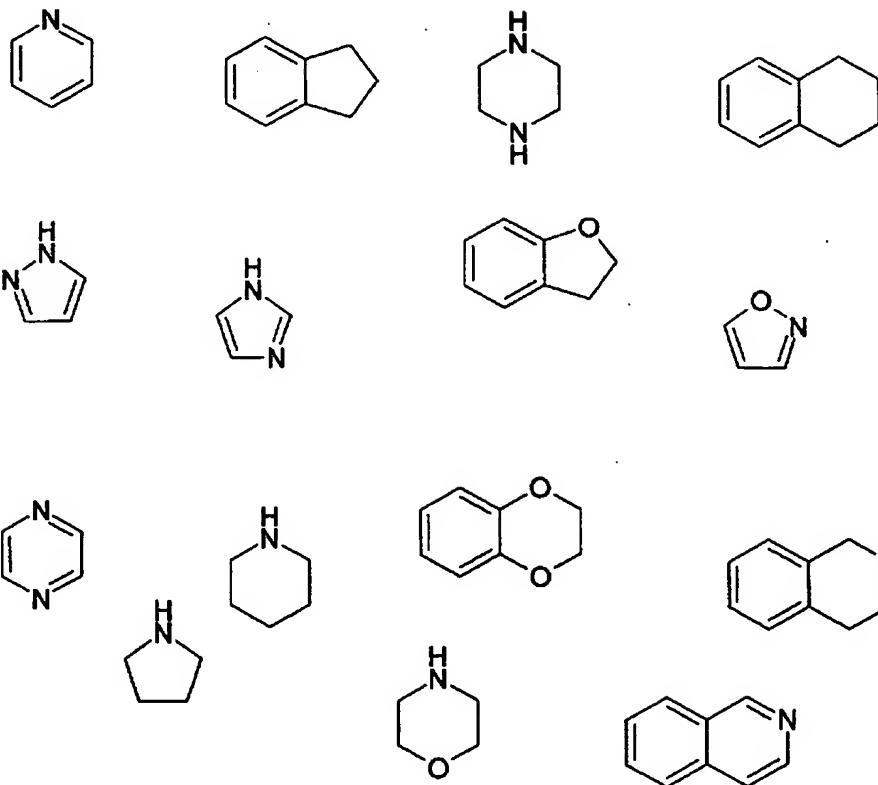
19. (Previously presented) A compound according to claim 1, wherein R^{29a} is selected from the group consisting of R^{29b}; and Z¹; and wherein Z¹ is selected from the group consisting of T¹; and T².

20. (Previously presented) A compound according to claim 1, wherein T¹ is phenyl; and wherein T¹ is optionally substituted with 1-3 R³⁸, which are the same or different.

21. (Previously presented) A compound according to claim 1, wherein R³⁸ is independently selected from the group consisting of F; Cl; CN; CH₃; C₂H₅; CH₂CH₂CH₃; CH(CH₃)₂; CF₃; O-CH₃; O-C₂H₅; S-CH₃; SO₂NH₂; T³; and O-T³.

22. (Previously presented) A compound according to claim 1, wherein T² is selected from the group consisting of

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and wherein T² is optionally substituted with 1-2 R⁴¹, which are the same or different.

23. (Previously presented) A compound according to claim 1, wherein R⁴¹ is selected from the group consisting of OH; CH₃; and T³;

24. (Previously presented) A compound according to claim 1, wherein T³ is T⁴.

25. (Previously presented) A compound according to claim 1, wherein T⁴ is phenyl, wherein T⁴ is optionally substituted with 1-3 R⁶¹, which are the same or different.

26. (Previously presented) A compound according to claim 1, wherein R⁵¹ is independently selected from the group consisting of F; Cl; CH₃; C₂H₅; CH₂CH₂CH₃; CH(CH₃)₂; CF₃; O-CH₃; O-C₂H₅; S-CH₃; and SO₂NH₂.

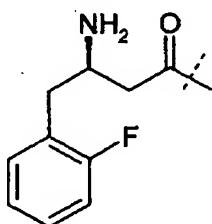
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27. (Previously presented) A compound according to claim 1, wherein T³ is T⁵.

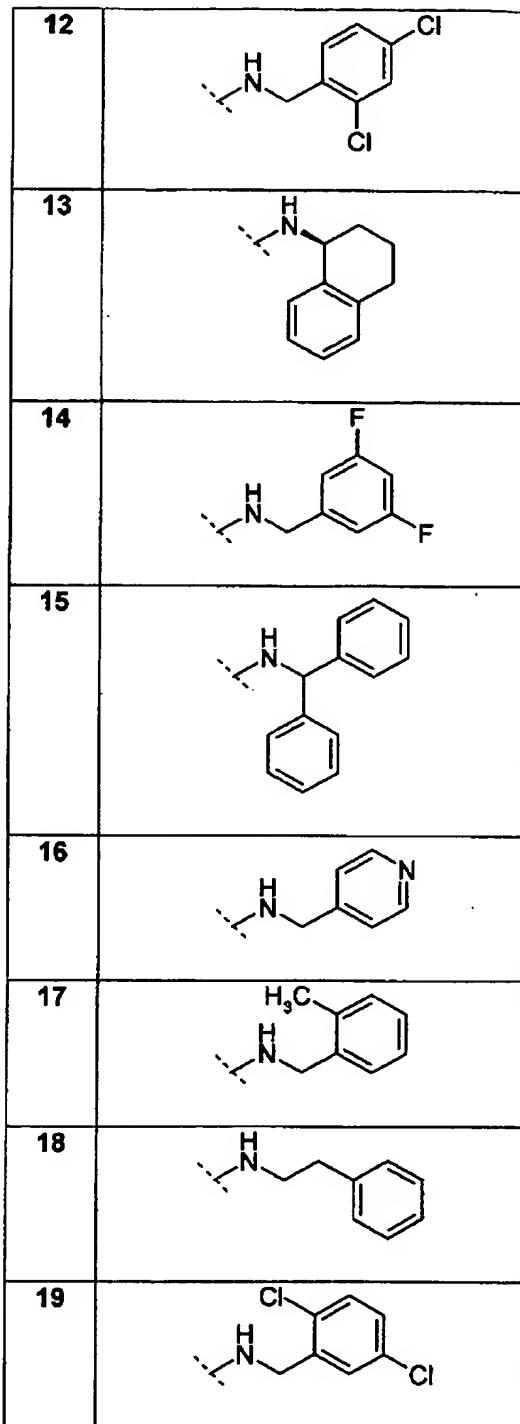
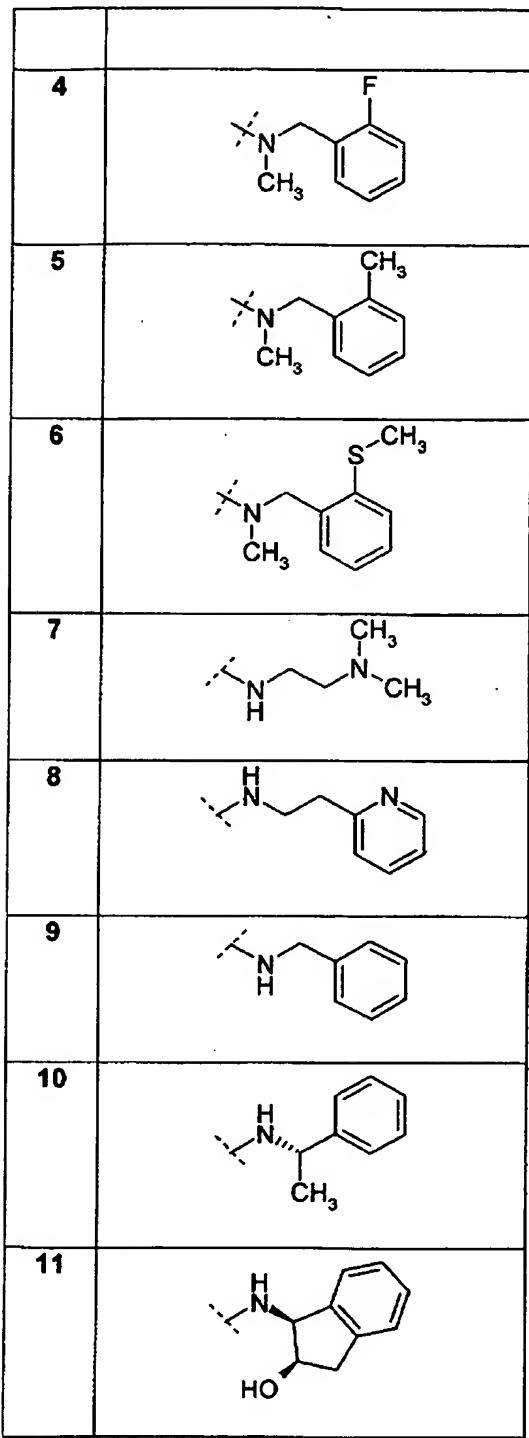
28. (Previously presented) A compound according to claim 1, wherein T⁵ is heterocycle,
wherein T⁵ is optionally substituted with 1-2 R⁵⁴, which are the same or different.

29. (Previously presented) A compound according to claim 1, wherein R⁵⁴ is selected
from the group consisting of OH; and CH₃.

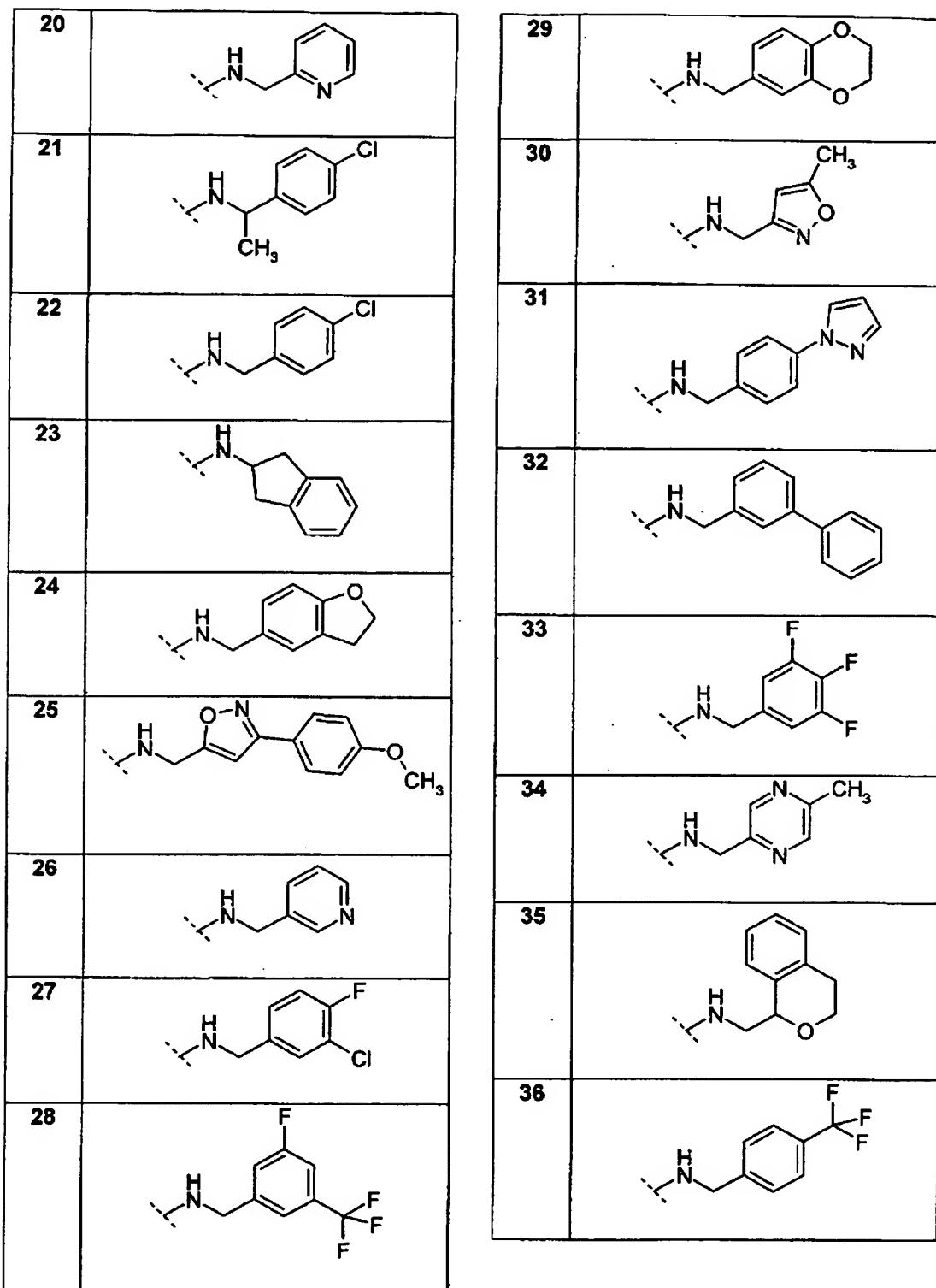
30. (Original) A compound according to claim 1 selected from the group consisting of



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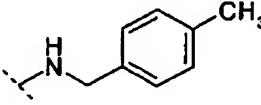
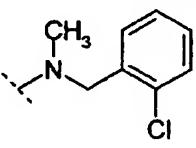
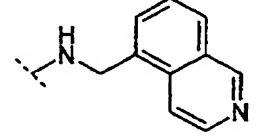
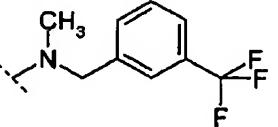
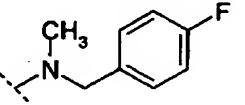
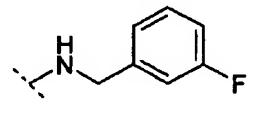
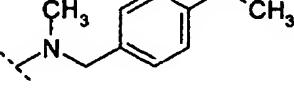
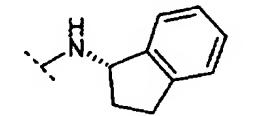
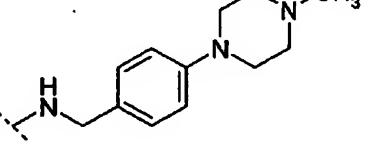
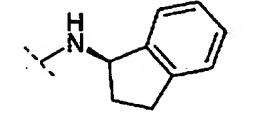
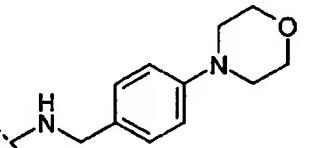
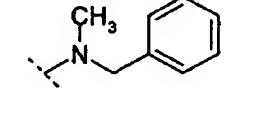
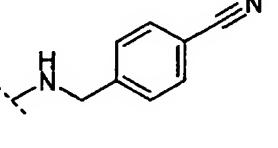
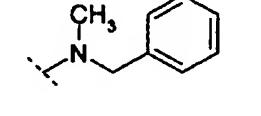
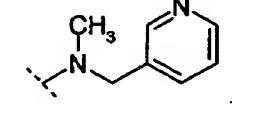
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31. (Previously presented) A prodrug compound of a compound according to claim 1.
32. (Currently amended) A pharmaceutical composition comprising said compound or said pharmaceutically acceptable salt thereof or a prodrug thereof according to claim 1 together with a pharmaceutically acceptable carrier.
33. (Currently amended) A pharmaceutical composition according to claim 32, comprising one or more additional compounds or pharmaceutically acceptable salts thereof selected from the group consisting of another of said compound or said pharmaceutically acceptable salt thereof or a prodrug thereof; another DPP-IV inhibitor; insulin sensitizers; PPAR agonists; biguanides; protein tyrosinephosphatase-IB (PTP-1B) inhibitors; insulin and insulin mimetics; sulfonylureas and other insulin secretagogues; α -glucosidase inhibitors; glucagon receptor antagonists; GLP-1, GLP-1 mimetics, and GLP-1 receptor agonists; GIP, GIP mimetics, and GIP receptor agonists; PACAP, PACAP mimetics, and PACAP receptor 3 agonists; cholesterol lowering agents; HMG-CoA reductase inhibitors; sequestrants; nicotinyl alcohol; nicotinic acid or a salt thereof; PPAR α agonists; PPAR γ dual agonists; inhibitors of cholesterol absorption; acyl CoA : cholesterol acyltransferase inhibitors; anti-oxidants; PPAR δ agonists; antiobesity compounds; an ileal bile acid transporter inhibitor; and anti-inflammatory agents.
34. (Currently amended) A compound or a pharmaceutically acceptable salt thereof or a prodrug thereof of claim 1 for use as a medicament.
35. (Currently amended) A method for the treatment or prophylaxis of non-insulin dependent (Type II) diabetes mellitus; hyperglycemia; obesity; insulin resistance; lipid disorders; dyslipidemia; hyperlipidemia; hypertriglyceridemia; hypercholesterolemia; low HDL; high LDL; atherosclerosis; growth hormone deficiency; diseases related to the immune response; HIV infection; neutropenia; neuronal disorders; tumor metastasis; benign

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prostatic hypertrophy; gingivitis; hypertension; osteoporosis; diseases related to sperm motility; low glucose tolerance; insulin resistance; ist sequelae; vascular restenosis; irritable bowel syndrome; inflammatory bowel disease; including Crohn's disease and ulcerative colitis; other inflammatory conditions; pancreatitis; abdominal obesity; neurodegenerative disease; anxiety; depression; retinopathy; nephropathy; neuropathy; Syndrome X; ovarian hyperandrogenism (polycystic ovarian syndrome; Type n diabetes; or growth hormone deficiency, comprising administering to a subject in need of said treatment said compound or said pharmaceutically acceptable salt thereof or a prodrug thereof of claim 1.

36. (Currently amended) A method to inhibit DPP-IV peptidase activity comprising administering said compound or said pharmaceutically acceptable salt thereof or a prodrug thereof of claim 1 to a subject in an amount sufficient to inhibit DPP-IV peptidase activity.